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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,067	05/23/2001	Thomas J. Meade	A-58762-20/RFT/RMS/RMK	7813

7590 04/21/2005

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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/866,067	MEADE ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 1/2005
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

FWL

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on January 31, 2005 has been entered. The claims pending in this application are claims 21-32. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of applicant's response filed on January 31, 2005.

Specification

2. The disclosure is objected to because of the following informality: (1) the amendment related to priority in page 2, lines 4-8 of applicant's remarks should not be used to replace the paragraph beginning at page 13, line 31 of the specification and should be used to add to the first sentence of the specification; and (2) the amendment related to Figure 2 in page 2, last paragraph of applicant's remarks should not be used to replace the paragraph beginning at page 13, line 31 of the specification and should be used to replace the first paragraph of page 14 of the specification.

Appropriate correction is required.

Claim Objections

3. Claims 22-26 are objected to because of the following informality: "A nucleotide" should be "the nucleotide".

4. Claims 28-32 are objected to because of the following informality: "A method" should be "the method".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 27-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 27 recites the limitation 'said modified nucleotide" in step b) of the claim. There is insufficient antecedent basis for this limitation in the claim because there is no "modified nucleotide" in step a) of the claim. Please clarify.

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 21-26 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Since, according to the specification, "electron donor moiety" and "electron acceptor moiety" are "molecules capable of electron transfer under certain conditions. It is to be understood that electron donor and acceptor capabilities are relative; that is, a molecule which can lose an electron under certain experimental conditions will be able to accept an electron

under different experimental conditions" (see page 15, lines 6-15), a hydroxyl group on the 2' position of the ribose (covalently attached) of ATP is an electron transfer moiety and ATP is a nucleotide triphosphate comprising a covalently attached electron transfer moiety as recited in claim 21. Since it is known that mammal cells produce ATP during tricarboxylic acid cycle, claims 21-26, as written, do not sufficiently distinguish over ATP as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught by page [insert page number] of specification. See MPEP 2105.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 24-26 and 27-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Although the specification describes 2' or 3' modified nucleotide triphosphate (see page 21, last paragraph) and deoxyribonucleoside triphosphates (see specification, page 40, first paragraph), the specification does not adequately describe that a nucleotide triphosphate comprising a covalently attached electron transfer moiety wherein said electron transfer moiety is a transition metal complex and said transition metal complex comprises a ruthenium atom or an iron atom as recited in claims 24-26 and any kind of modified nucleotide triphosphate as recited in claims 27-32. MPEP 2163.06 states that "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." In view of the embodiments adequately description in the specification, the subject application does not reasonably convey to one skilled in the art that applicant was in possession of the full scopes of products encompass in the claims at the time of the application was filled. Therefore, the written description requirement has not been satisfied.

In support of this position, attention is directed to the decision of *Vas-Cath inc. V. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

> This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 U.S.C. 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the "applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 21-23 and 27-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Inoue *et al.*, (US Patent No. 4,965,350, published on October 1990).

Inoue *et al.*, teach pyridopyrimidine nucleotide compounds.

Regarding claims 21-23, according to the specification, "electron donor moiety" and "electron acceptor moiety" are "molecules capable of electron transfer under certain conditions. It is to be understood that electron donor and acceptor capabilities are relative; that is, a molecule which can lose an electron under certain experimental conditions will be able to accept an electron under different experimental conditions" (see the specification, page 15, lines 6-15). Since 3-(5'-O-triphosphoryl-beta-D-deoxyribofuranosyl) 2,7-dioxopyrido[2,3-d]pyrimidine (see Examples 1-3 in columns 13-16) has three phosphates and a hydroxyl group on the 3' position of its ribose (covalently attached) and it is known that the hydroxyl group can donate a pair of electrons (see attachment for hydroxyl group, Schemes 1 and 2), 3-(5'-O-triphosphoryl-beta-D-deoxyribofuranosyl)2,7-dioxopyrido[2,3-d]pyrimidine is a nucleotide triphosphate as recited in claims 21 and 22. Since 3-(5'-O-triphosphoryl- beta-D-deoxyribofuranosyl) 2,7-dioxopyrido[2,3-d]pyrimidine is only one example of pyridopyrimidine nucleotide taught by Inoue *et al.*, 2'

position of the pyridopyrimidine nucleotide had W1 which can be either hydrogen or hydroxyl group (see column 2), the pyridopyrimidine nucleotide with a hydroxyl group on its 2' position taught by Inoue *et al.,* is a nucleotide triphosphate as recited in claim 23.

Regarding claims 27-29, since Inoue *et al.,* teach that 3-(5'-O-phosphoryl-beta-D-2'-deoxyribofuranosyl)-2,7-dioxopyrido[2,3-d]pyrimidine (see column 14) has a phosphate and a hydroxyl group on the 3' position of its ribose (covalently attached) and it is known that the hydroxyl group can donate a pair of electrons (see attachment for hydroxyl group, Schemes 1 and 2), 3-(5'-O-phosphoryl-beta-D-2'-deoxyribofuranosyl)-2,7-dioxopyrido[2,3-d]pyrimidine is a nucleotide as recited in step a) of claim 27. Since 3-(5'-O-phosphoryl-beta-D-2'-deoxyribofuranosyl)-2,7-dioxopyrido[2,3-d]pyrimidine is used to synthesize 3-(5'-O-triphosphoryl-beta-D-deoxyribofuranosyl)2,7-dioxopyrido[2,3-d]pyrimidine wherein 3-(5'-O-triphosphoryl-beta-D-deoxyribofuranosyl)2,7-dioxopyrido[2,3-d]pyrimidine (see Examples 1-3 in columns 13-16) has three phosphates and a hydroxyl group on the 3' position of its ribose (covalently attached) (see columns 13-16), and it is known that the hydroxyl group has a pair of electrons, 3-(5'-O-triphosphoryl-beta-D-deoxyribofuranosyl)2,7-dioxopyrido[2,3-d]pyrimidine is a modified nucleotide triphosphate as recited in step b) of claim 27 and claim 28, Inoue *et al.,* disclose providing a nucleotide comprising a covalently attached electron transfer moiety (ie., (5'-O-phosphoryl-beta-D-2'-deoxyribofuranosyl)-2,7-dioxopyrido[2,3-d]pyrimidine) and converting said nucleotide into a modified nucleotide triphosphate (ie., 3-(5'-O-triphosphoryl-beta-D-deoxyribofuranosyl)2,7-dioxopyrido[2,3-d]pyrimidine) as recited in steps a) and b) of claim 27. Since 3-(5'-O-triphosphoryl-beta-D-deoxyribofuranosyl)2,7-dioxopyrido[2,3-d]pyrimidine is used for synthesis of the dodecamers containing a fluorescent pyrimidine

nucleotide (see Figure 1 and example 4 in columns 16-18), Inoue *et al.*, disclose incorporating said modified nucleotide triphosphate in a synthetic reaction to form a nucleic acid with a covalently attached electron transfer moiety (ie., dodecamers containing a fluorescent pyrimidine nucleotide) as recited in step c) of claim 27. Besides 3-(5'-O-triphosphoryl- beta-D-deoxyribofuranosyl) 2,7-dioxopyrido[2,3-d]pyrimidine, Inoue *et al.*, teach other pyridopyrimidine nucleotide wherein X_1, Y_1, Z_1, W_1, R_1 and R_2 can be different atoms or groups (see (I) in column 2). When X_1, Y_1, Z_1, R_1 and R_2 of (I) and 3-(5'-O-triphosphoryl- beta-D-deoxyribofuranosyl) 2,7-dioxopyrido[2,3-d]pyrimidine are identical and W_1 of (I) is a hydroxyl group, (I) becomes 3-(5'-O-triphosphoryl- beta-D-ribofuranosyl) 2,7-dioxopyrido[2,3-d]pyrimidine. Therefore, Inoue *et al.*, teach that said electron transfer moiety (ie., W_1 of (I) is a hydroxyl group) is attached to the ribose via a linker at the 2' position as recited in claim 29.

Therefore, Inoue *et al.*, teach all limitations recited in claims 21-23 and 27-29.

Response to Arguments

In page 5, third paragraph bridging to page 10, first paragraph of applicant's remarks, applicant argues that (1) "hydroxyl groups should not be considered as ETMs" in view of the references from Hampson *et al.*, Gao *et al.*, Ramirez-Garcia *et al.*, Dang *et al.*, and Fussing *et al.*, and (2) "[A]pplicants contend that a molecule or pendant group can be considered to be an ETM if that molecule or pendant group can be induced to donate or accept an electron under the conditions disclosed in the present application. In the case of the present invention, such conditions comprise voltages in the range commonly used in electron transfer or electrochemistry experiments, e.g., from approximately -1 volt to +1 volt. Voltages beyond these extremes are not commonly explored because aqueous solvents break down outside this voltage range".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, according to the specification, "electron donor moiety" and "electron acceptor moiety" are "molecules capable of electron transfer under certain conditions. It is to be understood that electron donor and acceptor capabilities are relative; that is, a molecule which can lose an electron under certain experimental conditions will be able to accept an electron under different experimental conditions" (see page 15, lines 6-15). Since 3-(5'-O-triphosphoryl-beta-D-deoxyribofuranosyl) 2,7-dioxopyrido[2,3-d]pyrimidine taught by Inoue *et al.*, has three phosphates and a hydroxyl group on the 2' position of its ribose (covalently attached) (see column 16) and it is known that the hydroxyl group can donate a pair of electrons (see attachment for hydroxyl group, Schemes 1 and 2), Inoue *et al.*, teach a nucleotide triphosphate comprising a covalently attached electron transfer moiety (ie., the hydroxyl group

on the 2' position of the ribose of 3-(5'-O-triphosphoryl-beta-D-deoxyribofuranosyl) 2,7-dioxopyrido[2,3-d]pyrimidine) wherein said electron transfer moiety is attached to the ribose of said nucleotide and said electron transfer moiety is attached to the ribose via a linker at the 2' position as recited in claims 21-23. Second, there is no specific voltage range in the claims.

14. Claims 21-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Lehninger (Biochemistry, second edition, published on October 1975).

Regarding claims 21-23, according to the specification, "electron donor moiety" and "electron acceptor moiety" are "molecules capable of electron transfer under certain conditions. It is to be understood that electron donor and acceptor capabilities are relative; that is, a molecule which can lose an electron under certain experimental conditions will be able to accept an electron under different experimental conditions" (see the specification, page 15, lines 6-15). Since NTP taught by Lehninger has three phosphates and a hydroxyl group on the 2' position of its ribose (covalently attached) (see page 315) and it is known that the hydroxyl group can donate a pair of electrons (see attachment for hydroxyl group, Schemes 1 and 2), Lehninger teaches a nucleotide triphosphate comprising a covalently attached electron transfer moiety (ie., the hydroxyl group on the 2' position of the ribose of NTP) wherein said electron transfer moiety is attached to the ribose of said nucleotide and said electron transfer moiety is attached to the ribose via a linker at the 2' position as recited in claims 21-23.

Therefore, Lehninger teaches all limitations recited in claims 21-23.

Conclusion

15. No claim is allowed.

16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (703)872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (571)272-0745.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
April 14, 2005

FRANK LU
PATENT EXAMINER